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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,614	02/06/2006	Stefan Golz	Le A 36 493	6701

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/537,614	GOLZ ET AL.	
	Examiner	Art Unit	
	SCOTT D. LONG	1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 March 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *5* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *1 and 7*.
   Claim(s) rejected: *1-4,6 and 8-12*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Janet L. Epps-Ford/
Primary Examiner, Art Unit 1633

Continuation of 11. does NOT place the application in condition for allowance because:

The proposed claim amendments do not simplify matters for appeal or allowance. In fact, no amendments were submitted which overcome the outstanding rejections. Rather, the applicant has merely presented further arguments directed to the pending claims. The new claims that are presented, are either identical to cancelled claims (claims 13 and 16) or a substantial duplicate claim (claim 15 claims the same subject matter as claim 1) or claims a single member of a markush group (claim 14). Therefore, the new claims also do not simplify matters. Therefore the proposed claim set will not be admitted.

If admitted, the claims amendments would overcome the claim objections would be overcome.

The instant claims remain rejected for the reasons of record and the comments below. The applicant has offered further arguments that have been addressed in the previous actions. Since prosecution is closed, the examiner will only briefly address the 19 pages of arguments submitted by the applicant.

35 USC 112, 1st (Written Description)

The applicant makes 4 arguments regarding the written description rejections:

(1) Because the art knows the structure and function of each and every amino acid in GFP, therefore the applicant is in possession of the claimed genus of nucleic acids sharing homology to SEQ ID NO:1 and to nucleic acids encoding proteins sharing homology to SEQ ID NO: 2. While many variants of GFP are known in the art, the applicant claims that their nucleic acid sequence SEQ ID NO:1 and amino acid sequence SEQ ID NO:2 are novel and have excitation and emission spectra which differs from other known GFPs. Since this distinct characteristic is critical to the claimed invention and the specification does not describe which particular amino acids are essential for the unique excitation and emission spectra, the examiner concludes that a skilled artisan would not believe the applicant was in possession of a genus of molecules 95% homologous to the claimed GFP. Therefore, the examiner finds the arguments on pages 7-13 of Remarks (filed 3/3/2008) unpersuasive. Therefore, claims 1, 2, 3, 6, 13 (formerly claim 7) and 16 (formerly claims 8) remain rejected under 35 USC 112, 1st paragraph (written description).

(2) The applicant argues "written description for a genus of antibodies is found so long as the specification provides a well-defined antigen since antibody prepraration and technology is routine in the art" (Remarks, page 13). To support his position, the applicant refers to Example 16 of the Written Description Guidelines. The specification's only mention of antibodies directed to the whole GFP or portions of the GFP claimed by the applicants is "The invention related to peptides, having more than 5 continguous amino acids which are recognized immunologically by antibodies to the fluorescent protein according to the invention" (page 13, lines 10-12). The examiner notes that this is not an explicit recitation of antibodies immunogenic against the fluorescent proteins of the instant invention; rather it is a recitation of peptides which could be recognized by a variety of commercially available antibodies. This is especially true because the exact epitopes are not described and many antibodies are available which recognize other GFPs. As mentioned in the previous action, the specification contains no specific claim of an antibody (in originally filed claim set) or description of an embodiment of an antibody immunogenic against the claimed fluorescent protein. For that reason, the examiner concluded there is no written description. The examiner did not explicitly identify claim 9 as new matter, but it is not supported by the teachings of specification. However, if claim 14 is admitted, it will be rejected under New Matter. Therefore, claim 9 remains rejected under 35 USC 112, 1st paragraph (WD).

(3) The applicant argues that claim 10 is not new matter, because while the exact steps of amended claim 10 were not taught in the instant specification, claim 10 recites steps which are "merely conventional steps well-known in the art for using any fluorescent protein as a marker gene or reporter gene" (Remarks, page 15). The examiner enjoyed reading this argument and hopes this becomes case law, since it would be very helpful in obviousness art rejections. Unfortunately, the examiner believes that actual support in the specification is required in order for a method containing specific steps can be considered for allowance. since these "conventional steps" are not recited in the specification, the examiner remains convinced that there is no support in the specification and it is new matter. Therefore, the claim 10 remains rejected under New Matter.

(4) The applicant argues that because they have overcome the written description rejection for claim 1, that they have also overcome the WD rejection for dependent claims 4, 11, and 12. The examiner has maintained the rejection of claim 1, so he likewise maintains the rejection of claims 4, 11 and 12 under 35 USC 112, 1st (WD).

35 USC 102(b)

Claim 6 remains rejected under 35 USC 102(b) as anticiapted by Levine et al (Compar. Biochem. Physiol. B, 1982. 72; 1:77-86).

The applicant argues that the GFP taught by Levine is not the same as the fluorescent protein of instantly claimed SEQ ID NO:2. Specifically, the applicant states, "LEVINE did not provide a purified green fluorescent [protein]...did not provide or determine the amino acid sequence of its green fluorescent protein, and did not provide the corresponding nucleic acid sequence. (Remarks, page 18). The examiner agrees with the applicant's assertion that Levine et al. do not provide a nucleic acid sequence or amino acid sequence for the Green Fluorescent protein described in their reference. However, claim 6 recites "an isolated protein encoded by the nucleic acid molecule of claim 1." Although the applicant has defined their GFP using SEQ ID NOs, Levine isolated their GFP using protein purification methods

in 1982, rather than to more recent molecular biological methods commonly used today. Nevertheless, if the Levine protein is the same protein as that of claim 6, as asserted by the examiner, then Levine would inherently satisfy the sequence related claim language. In addition, Levine et al. teach "isolation and characterization of...a spectrally unique green-fluorescent protein" (title). Therefore, the examiner finds this argument unpersuasive.

The applicant attempts to prove that the Levine GFP and the instantly claimed GFP are different proteins. While the applicant acknowledges that both the applicant and Levine isolated their green fluorescent proteins from the same organism, the applicant contends that they are not the same protein. The applicant proposes that they might be different fluorescent proteins within the same organism. The applicant provides several facts to support his posistion.

The applicant cites the molecular weight of the Levine GFP as 57,000 +/- 4% grams/mol (as determined by gel filtration), while indicating that the SEQ ID NO:2 GFP is 26,385.0 grams/mole (as determined by x-ray crystalography). Levine discusses the variations between their methods and those of other laboratories when measuring the apparent molecular weights of other GFPs in the same paragraph as that revealing their estimation of P-GFP to be 57,000 +/- 4% grams/mol. The implication is that their measurement may not be completely accurate. In fact, Levine et al. suggest that the apparent molecular weights may vary by 20 to 50% (page 80, col.1, 2nd parag to col.2, top). Therefore, the examiner does not conclude that the discepancy between the molecular weights presented by Levine and the applicant is a persuasive argument.

The applicant provides a comparison of the excitation and emission spectra for both SEQ ID NO:2 and P-GFP (Levine) in Schematic 1 (Remarks, page 20). The applicant makes several conclusions based on the data shown in Schematic 1. The applicant concludes that the "shoulder-peak at around 425 nm" is a significant difference between the two proteins. The examiner reminds the applicant that there is a control in the application's Figure 4 with a peak at bout 425 nm. If this "background" were subtracted, the "shoulder-peak" would be eliminated, thereby smoothing the applicant's curve to match that of the Levine GFP. In addition, the applicant points out the apparent difference between the double peak of excitation (shown in Fig.4 of the specification) and the single peak of excitation shown in Levine. The double peak in the application's GFP excitation profile is not a characteristic of a single fluorescent protein. In fact, since it is clear that there are contaminating fluorescent proteins, excited at about 435 nm, the examiner concludes that there are either two different proteins having close, but not identical excitation wavelengths or two variant forms of the the same protein. Therefore, the examiner believes this difference in profiles is not a convincing argument that SEQ ID NO:2 and P-GFP are different proteins. Regarding the estimation of excitation and emission makimums (discussed on Remark, page 21), the examiner reminds the applicant that the examiner used his eyeballs to estimate the excitation and emission maximum of SEQ ID NO:2, since the instant application does not specifically state this data. Therefore the very small difference between the spectra for the GFP of Levine and the GFP of SEQ ID NO:2 can be attributed to the examiner's poor eyesight and the resolution of the Figures. In elaborating on the difference between the maximum peaks of P-GFP and that of SEQ ID NO:2, the applicant also bases part of his analysis on the eyeball estimation of the examiner. Therefore, the examiner finds the applicant's arguments unpersuasive.

Finally, the applicant reiterates his assertion that Levine does not teach an isolated GFP, its amino acid and nucleic acid sequences. As stated above, the instant claim is directed to an isolated protein. The examiner believes that Levine inherently teaches the isolated protein of SEQ ID NO:2, for the reasons of record and the comments above. Therefore, the examiner hereby maintains the rejection of claim 6 as anticipated by Levine.

/SDL/ Scott Long
Patent Examiner, AU 1633